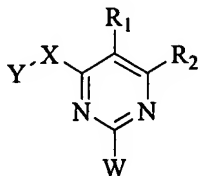


AMENDMENTS TO THE CLAIMS

1. (Currently amended) A compound having the formula I:



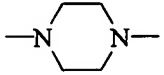
(I)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- ~~(1) substituted or unsubstituted C₁-C₆ alkyl,~~
- ~~(2) substituted or unsubstituted C₂-C₆ alkenyl,~~
- ~~(3) substituted or unsubstituted C₂-C₆ alkynyl,~~
- [[(4)]] (1) substituted or unsubstituted aryl,
- [[(5)]] (2) substituted or unsubstituted heterocyclyl, and
- [[(6)]] (3) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) -N(R^{1x})-,
- (3) -(CH₂)_m-C(R^{2x}, R^{3x})-N(R^{1x})-,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) -SO₂-,
- (8) -C(R^{2x}, R^{3x})-, and
- (9) ,

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) -OR^{1t}, and
- (6) -NHR^{1t},

wherein R^{1t} is H or C₁-C₆-alkyl;

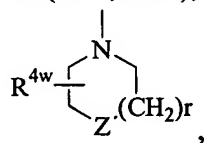
R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- ~~(3) substituted or unsubstituted heterocyclyl; and~~

W is selected from the group consisting of

- ~~(1) substituted or unsubstituted C₁-C₆-alkyl,~~

[[(2)]] (1) -N(R^{1w}, R^{2w}), and



[[(3)]] (2)

wherein R^{1w} and R^{2w} are selected from the group consisting of

- ~~(a) H,~~
- ~~(b) substituted or unsubstituted C₁-C₆-alkyl,~~

- [[(c)] (a) substituted or unsubstituted aryl,
 [[(d)] (b) substituted or unsubstituted heterocyclyl, and
 [[(e)] (c) substituted or unsubstituted heteroaryl,
 wherein R^{1w} and R^{2w} are not both H;

Z is selected from the group consisting of

- (a) -O-,
 (b) -NR^z-,
 (c) -S-,
 (d) -SO-,
 (e) -SO₂-, and
 (f) -CH₂-,

wherein R^z is H or substituted or unsubstituted alkyl group; and

R^{4w} is selected from the group consisting of

- (a) H,
 (b) substituted or unsubstituted C₁-C₆-alkyl,
 (c) -COOR^{5w},
 (d) -CONH₂,
 (e) -OR^{5w}, and
 (f) -NHR^{5w},

wherein R^{5w} is H or C₁-C₆-alkyl; and r is 0, 1, or 2;

~~with the proviso that when X is O, then Y is substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, or substituted or unsubstituted heteroaryl;~~

~~with the proviso that when W is morpholino, thiomorpholino, 1-oxide thiomorpholino, 1,1-dioxido morpholino, piperazino, or N-substituted piperazino, R₂ is morpholino, thiomorpholino, 1-oxide thiomorpholino, 1,1-dioxido thiomorpholino, piperazino, or N-[acetyl(alkanoyl of 1 to 3 carbon atoms)]piperazino, and X is NH, then Y is not hydrogen, alkyl of 1 to 3 carbon atoms, cyclohexyl, phenyl, chloro phenyl, carboxy phenyl, carbomethoxy phenyl, or pyridyl;~~

~~with the proviso that when W is morpholino, thiomorpholino, 1-oxide-thiomorpholino, 1,1-dioxido-morpholino, piperazino, or N-substituted piperazino, R₂ is morpholino, thiomorpholino, 1-oxide-thiomorpholino, 1,1-dioxido-thiomorpholino, piperazino, or N'-[acetyl(alkanoyl of 1 to 3 carbon atoms)]piperazino, and X is a direct link, then Y is not phenyl, substituted or unsubstituted C₁-C₆-alkyl, or 1-oxidethiomorpholino; and~~

with the proviso that when R₂ is phenyl independently substituted with one to five substituents selected from hydrogen, cycloalkyl, heterocycloalkyl, halo, nitro, amino, sulphonamido, or alkylsulphonylamino, R₁ is hydrogen, haloalkyl, alkyl, or halo, and X is NR^{1x}, then Y is substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocyclyl.

2. (Currently amended) The compound of claim 1, wherein

Y is selected from the group consisting of

~~(1) —substituted or unsubstituted C₁-C₆-alkyl;~~

[[~~(2)~~]] (1) substituted or unsubstituted aryl,

[[~~(3)~~]] (2) substituted or unsubstituted heterocyclyl, and

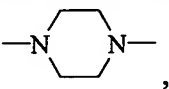
[[~~(4)~~]] (3) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

(1) a direct link,

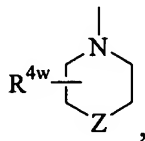
(2) -N(R^{1x})-,

(3) -(CH₂)_m-C(R^{2x}, R^{3x})-N(R^{1x})-, and

(4) ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C₁-C₆-alkyl; and

W is selected from the group consisting of



wherein Z is -O- or -NR^z-, wherein R^{4w} is H or substituted or unsubstituted C₁-C₆-alkyl.

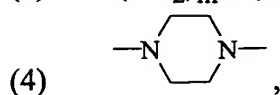
3. (Original) The compound of claim 1, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted heterocyclyl,
- (2) substituted or unsubstituted heteroaryl;

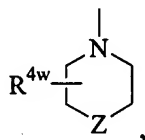
X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and



wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted C_1 - C_6 -alkyl; and

W is selected from the group consisting of



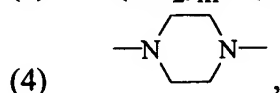
wherein Z is $-O-$ or $-NR^Z-$, wherein R^{4w} is H or substituted or unsubstituted C_1 - C_6 -alkyl.

4. (Original) The compound of claim 1, wherein

Y is substituted or unsubstituted aryl;

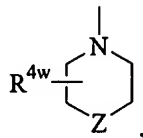
X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and



wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted C_1 - C_6 -alkyl; and

W is selected from the group consisting of

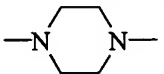


wherein Z is -O- or -NR^z-, wherein R^{4w} is H or substituted or unsubstituted C₁-C₆-alkyl.

5. (Currently amended) The compound of claim 1, wherein

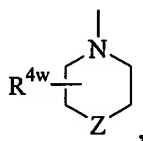
~~Y is substituted or unsubstituted alkyl;~~

X is selected from the group consisting of

- (1) a direct link,
- (2) -N(R^{1x})-,
- (3) -(CH₂)_m-C(R^{2x}, R^{3x})-N(R^{1x})-, and
- (4) ,

wherein R^{1x}, R^{2x}, R^{3x} are independently H or substituted or unsubstituted C₁-C₆-alkyl; and

W is selected from the group consisting of



wherein Z is -O- or -NR^z-, wherein R^{4w} is H or substituted or unsubstituted C₁-C₆-alkyl.

6. (Original) The compound of claim 1, wherein

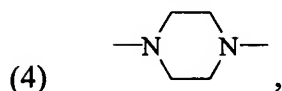
Y is selected from the group consisting of

- (1) substituted or unsubstituted heterocyclyl,
- (2) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) -N(R^{1x})-,

(3) $-(\text{CH}_2)_m-\text{C}(\text{R}^{2x}, \text{R}^{3x})-\text{N}(\text{R}^{1x})-$, and

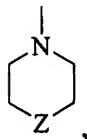


wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted

$\text{C}_1\text{-C}_6$ -alkyl;

R_2 is substituted or unsubstituted aryl; and

W is



wherein Z is -O- or -NH-.

7. (Original) The compound of claim 1, wherein

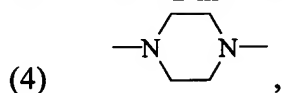
Y is substituted or unsubstituted aryl;

X is selected from the group consisting of

(1) a direct link,

(2) $-\text{N}(\text{R}^{1x})-$,

(3) $-(\text{CH}_2)_m-\text{C}(\text{R}^{2x}, \text{R}^{3x})-\text{N}(\text{R}^{1x})-$, and

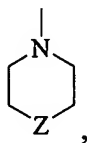


wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted

$\text{C}_1\text{-C}_6$ -alkyl;

R_2 is substituted or unsubstituted aryl; and

W is



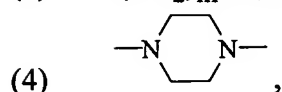
wherein Z is -O- or -NH-.

8. (Currently amended) The compound of claim 1, wherein

~~Y is substituted or unsubstituted alkyl;~~

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

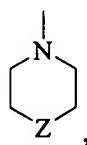


wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted

C_1 - C_6 -alkyl;

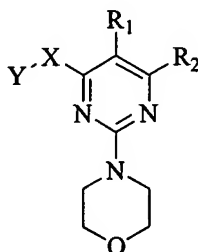
R_2 is substituted or unsubstituted aryl; and

W is



wherein Z is -O- or -NH-.

9. (Currently amended) The compound of claim 1, having the formula II:



(II)

wherein Y is selected from the group consisting of

~~(1) substituted or unsubstituted C_1 - C_6 -alkyl,~~

[[(2)]] (1) substituted or unsubstituted aryl,

[[(3)]] (2) substituted or unsubstituted heterocyclyl, and

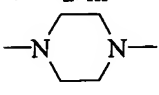
[[(4)]] (3) substituted or unsubstituted heteroaryl; and

X is selected from the group consisting of

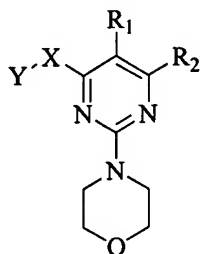
(1) a direct link,

(2) $-N(R^{1x})-$,

(3) $-(\text{CH}_2)_m-\text{C}(\text{R}^{2x}, \text{R}^{3x})-\text{N}(\text{R}^{1x})-$, and

(4) 

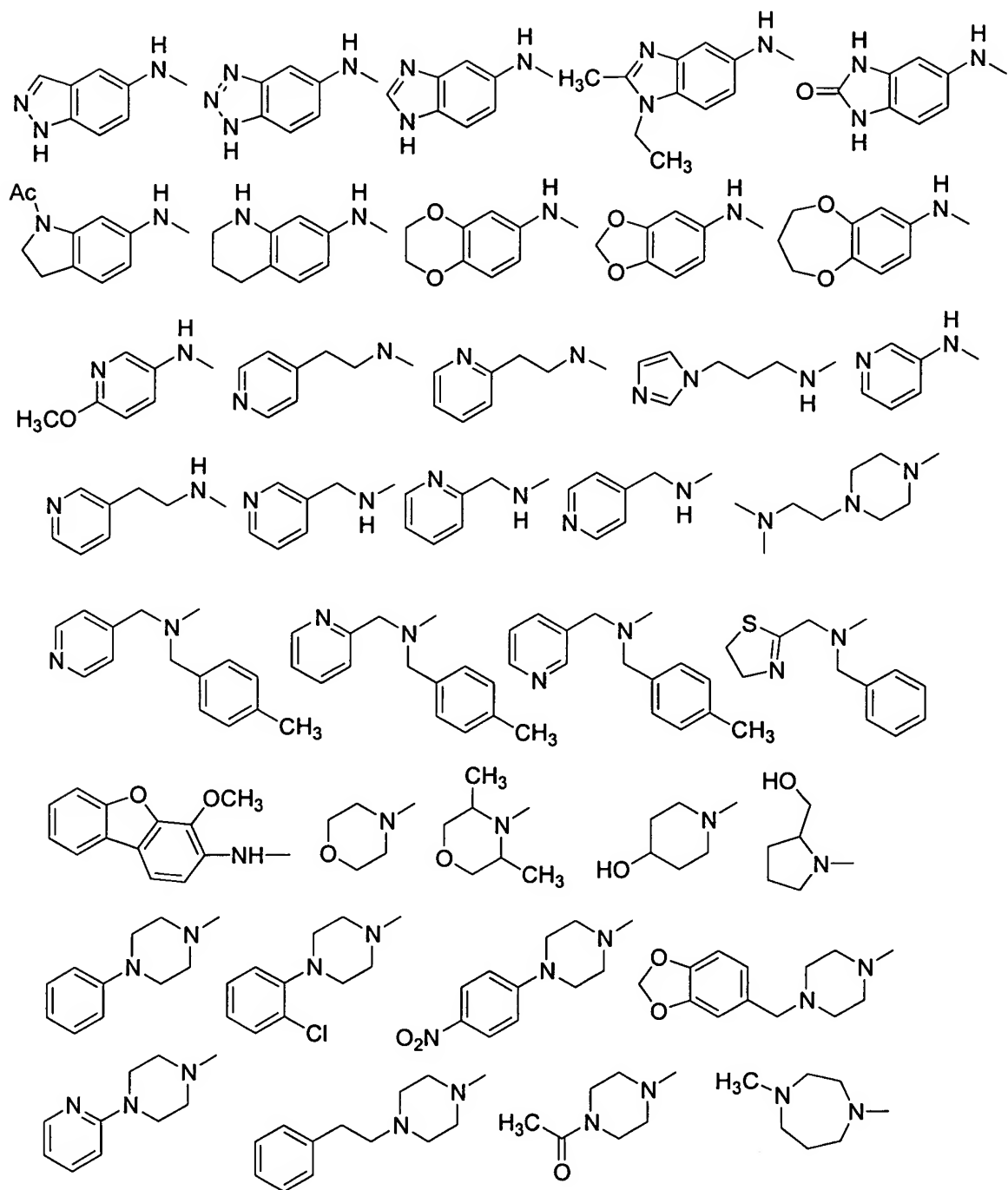
10. (Original) The compound of claim 1, having the formula II:



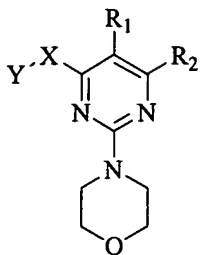
(II)

wherein Y and X, taken together, are selected from the group consisting of

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CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

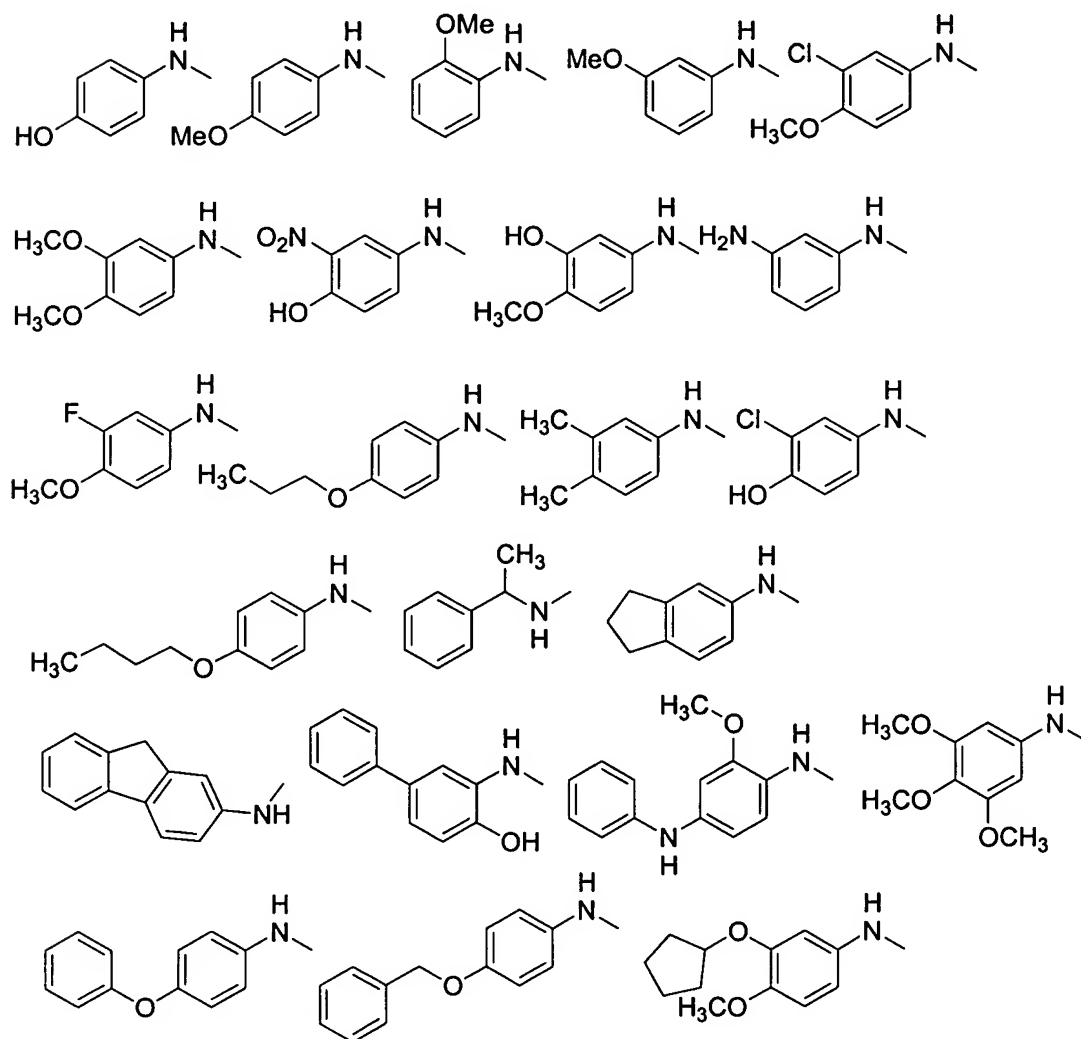


11. (Original) The compound of claim 1, having the formula II:

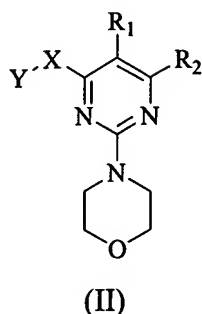


(II)

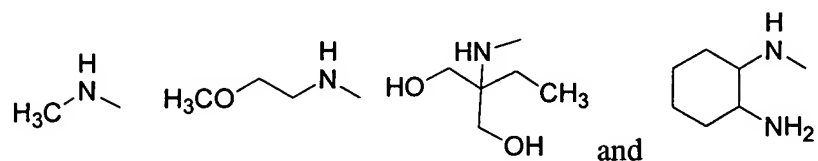
wherein Y and X, taken together, are selected from the group consisting of



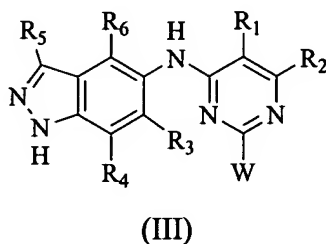
12. (Original) The compound of claim 1, having the formula II:



wherein, Y and X, taken together, are selected from the group consisting of



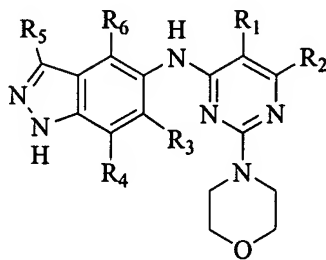
13. (Currently amended) The compound of claim 1, having the formula III:



wherein R₃, R₄, R₅, R₆ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOR^{1t},
- (4) ~~COONH₂~~ -CONH₂,
- (5) -OR^{1t}, and
- (6) -NHR^{1t}.

14. (Currently amended) The compound of claim 1, having the formula IV:

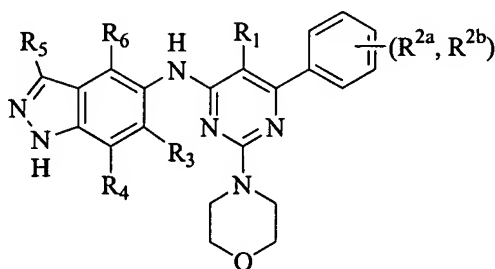


(IV)

wherein R₃, R₄, R₅, R₆ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOR^{1t},
- (4) ~~COONH₂~~ CONH₂
- (5) -OR^{1t}, and
- (6) -NHR^{1t}.

15. (Currently amended) The compound of claim 1, having the formula V:



(V)

wherein R₃, R₄, R₅, R₆ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOR^{1t},
- (4) ~~COONH₂~~ CONH₂
- (5) -OR^{1t}, and

(6) -NHR^{1t} ; and

R^{2a} and R^{2b} are selected from the group consisting of

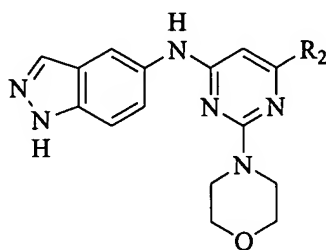
- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) halo,
- (4) $\text{-(CH}_2)_q\text{-N(R}^{2c}, \text{R}^{2d})$,
- (5) $\text{-(CH}_2)_q\text{-N(R}^{2c}, \text{R}^{2d})\text{COR}^{2e}$,
- (6) $\text{-(CH}_2)_q\text{-OR}^{2e}$,
- (7) $\text{-(CH}_2)_q\text{-OCOR}^{2e}$,
- (8) $\text{-(CH}_2)_q\text{-OCOOR}^{2e}$,
- (9) $\text{-(CH}_2)_q\text{-COOR}^{2e}$,
- (10) $\text{-(CH}_2)_q\text{-CONR}^{2c}$,
- (11) -CN ,
- (12) -NO_2 ,
- (13) $\text{-SO}_2\text{NH}_2$,
- (14) $\text{-NHSO}_2\text{CH}_3$, and
- (15) $\text{-SO}_2\text{R}^{2f}$,

wherein R^{2c} , R^{2d} , R^{2e} , and R^{2f} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted phenyl; and

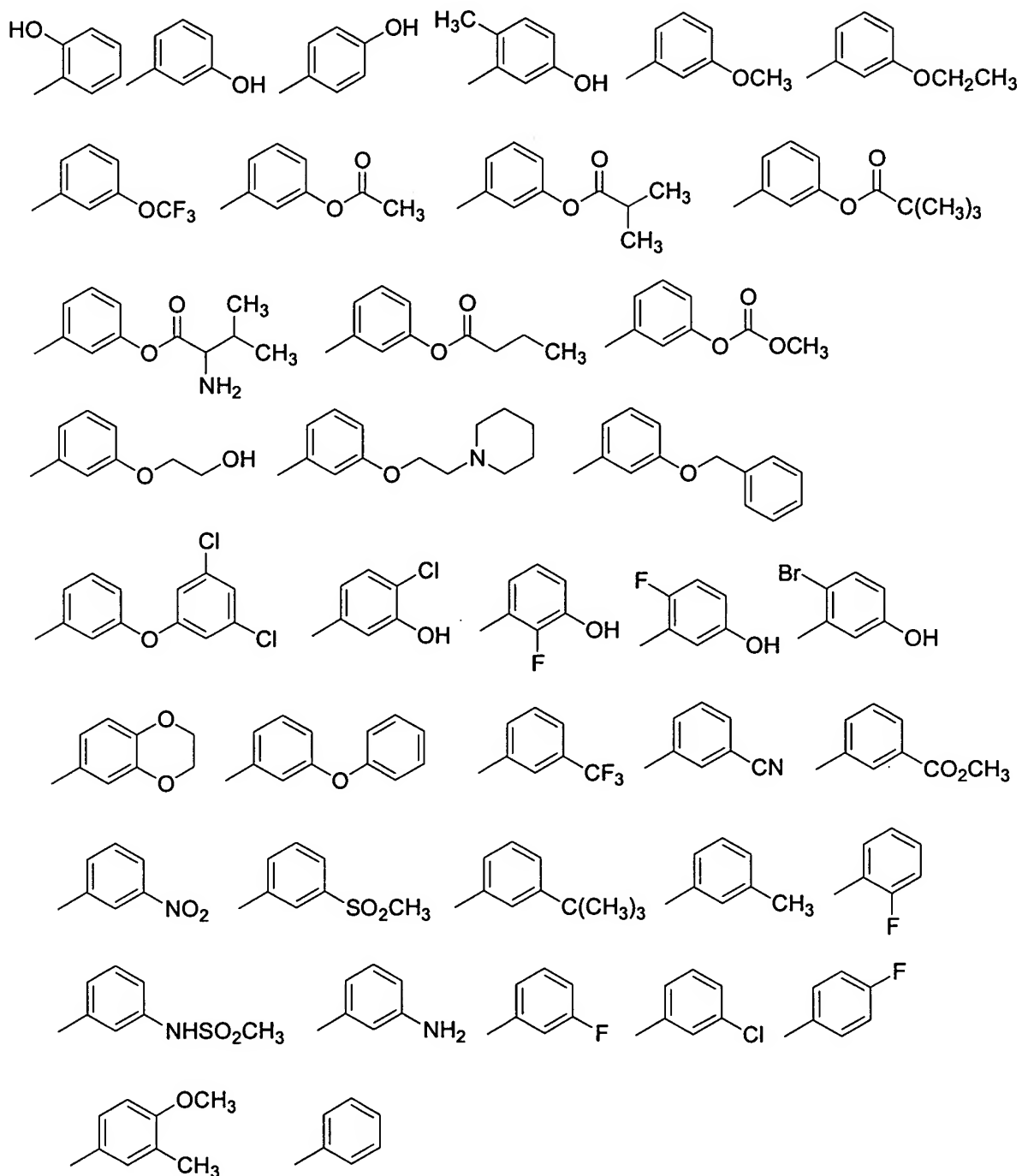
q is 0, 1, 2, 3, or 4.

16. (Original) The compound of claim 1, having the formula VI:

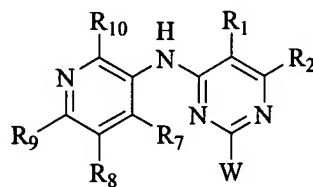


(VI)

wherein R₂ is selected from the group consisting of



17. (Currently amended) The compound of claim 1, having the formula VII:

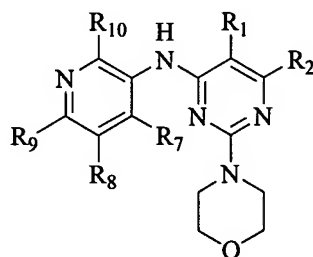


(VII)

wherein R₇, R₈, R₉, and R₁₀ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOR^{1t},
- (4) ~~COONH₂~~ CONH₂,
- (5) -OR^{1t}, and
- (6) -NHR^{1t}.

18. (Original) The compound of claim 1, having the formula VIII:

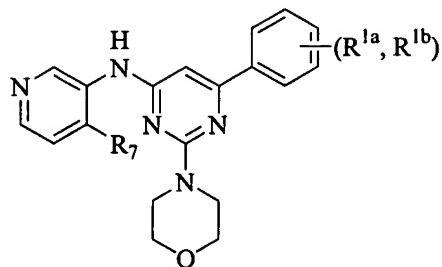


(VIII)

wherein R₇, R₈, R₉, R₁₀ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOR^{1t},
- (4) -CONH₂,
- (5) -OR^{1t}, and
- (6) -NHR^{1t}.

19. (Original) The compound of claim 1, having the formula IX:



(IX)

wherein R^{1a} and R^{1b} are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) halo,
- (4) $-(CH_2)_q-N(R^{2c}, R^{2d})$,
- (5) $-(CH_2)_q-N(R^{2c}, R^{2d})COR^{2e}$,
- (6) $-(CH_2)_q-OR^{2e}$,
- (7) $-(CH_2)_q-OCOR^{2e}$,
- (8) $-(CH_2)_q-OCOOR^{2e}$,
- (9) $-(CH_2)_q-COOR^{2e}$,
- (10) $-(CH_2)_q-CONR^{2c}$,
- (11) -CN,
- (12) -NO₂,
- (13) -SO₂NH₂,
- (14) -NHSO₂CH₃, and
- (15) -SO₂R^{2f},

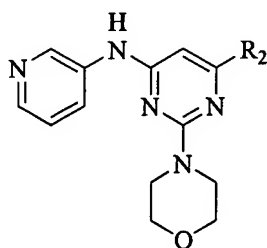
wherein R^{2c}, R^{2d}, R^{2e}, and R^{2f} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted phenyl; and

wherein R₇ is selected from the group consisting of

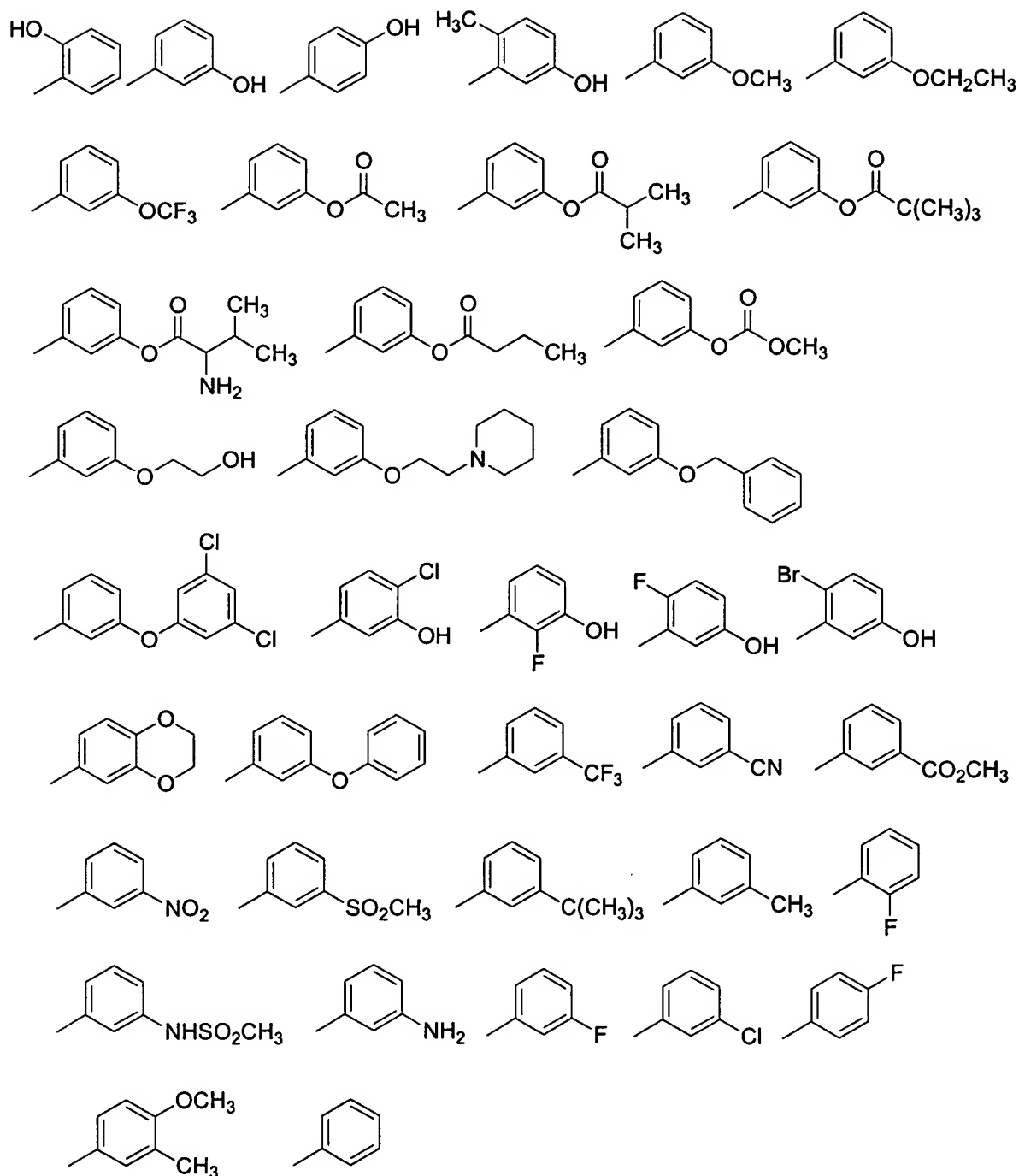
- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOR^{1t},
- (4) -CONH₂,
- (5) -OR^{1t}, and
- (6) -NHR^{1t}.

20. (Original) The compound of claim 1, having the formula X:

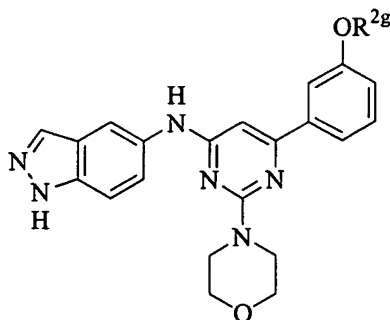


(X)

wherein R₂ is selected from the group consisting of



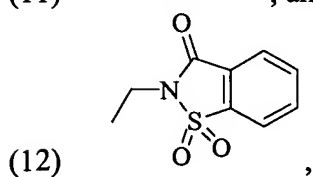
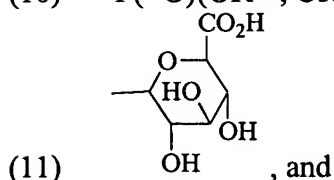
21. (Original) The compound of claim 1, having the formula XI:



(XI)

wherein R^{2g} is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) -CONHR^{2h},
- (4) -CON(R^{2h})-(CH₂)₂₋₃-N(R^{2h}, R²ⁱ),
- (5) -COR^{2j},
- (6) -CO₂R^{2j},
- (7) -COC₁-C₆-alkyl-CO₂H,
- (8) -CH₂-OC(=O)R²ⁱ,
- (9) -CH₂-OC(=O)NHCHR²ⁱCO₂R^{2j},
- (10) -P(=O)(OR^{2k}, OR^{2p}),

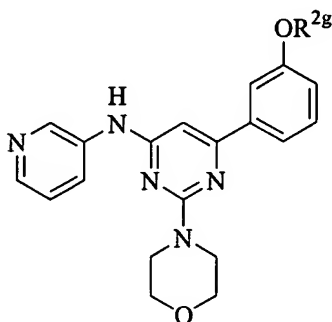


wherein R^{2h}, R²ⁱ, R^{2j}, R^{2k}, and R^{2p} are selected from the group consisting of

- (a) H,

- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted aryl.

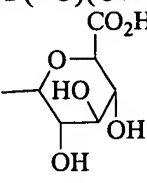
22. (Original) The compound of claim 1, having the formula XII:

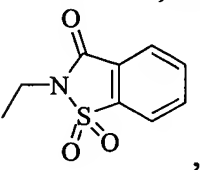


(XII)

wherein R^{2g} is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) -CONHR^{2h},
- (4) -CON(R^{2h})-(CH₂)₂₋₃-N(R^{2h}, R²ⁱ),
- (5) -COR^{2j},
- (6) -CO₂R^{2j},
- (7) -COC₁-C₆-alkyl-CO₂H,
- (8) -CH₂-OC(=O)R²ⁱ,
- (9) -CH₂-OC(=O)NHCHR²ⁱCO₂R^{2j},
- (10) -P(=O)(OR^{2k}, OR^{2p}),

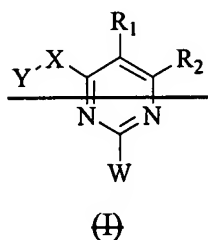
- (11) , and

- (12) ,

wherein R^{2h} , R^{2i} , R^{2j} , R^{2k} , and R^{2p} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted aryl.

23. (Currently amended) A composition, comprising a pharmaceutically acceptable carrier and an amount of a compound of Claim 1 effective to inhibit phosphatidylinositol (PI) 3-kinase activity in a human or animal subject when administered thereto, ~~wherein the compound has the formula I:~~



~~or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein~~

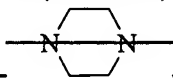
~~Y is selected from the group consisting of~~

- ~~(1) — substituted or unsubstituted C_1 - C_6 -alkyl,~~
- ~~(2) — substituted or unsubstituted C_2 - C_6 -alkenyl,~~
- ~~(3) — substituted or unsubstituted C_2 - C_6 -alkynyl,~~
- ~~(4) — substituted or unsubstituted aryl,~~
- ~~(5) — substituted or unsubstituted heterocyclyl, and~~
- ~~(6) — substituted or unsubstituted heteroaryl;~~

~~X is selected from the group consisting of~~

- ~~(1) — a direct link,~~
- ~~(2) — $N(R^{1*})$,~~
- ~~(3) — $(CH_2)_m-C(R^{2*}, R^{3*})-N(R^{1*})$,~~
- ~~(4) — O,~~
- ~~(5) — S,~~

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- (6) —SO—,
 (7) —SO₂—,
 (8) —C(R^{2*}, R^{3*})—, and
 (9) ——,

wherein R^{1*}, R^{2*}, and R^{3*} are selected from the group consisting of

- (a) —H,
 (b) —substituted or unsubstituted C₁–C₆–alkyl,
 (c) —substituted or unsubstituted C₂–C₆–alkenyl,
 (d) —substituted or unsubstituted C₂–C₆–alkynyl,
 (e) —substituted or unsubstituted aryl,
 (f) —substituted or unsubstituted heterocyclyl,
 (g) —substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) —H,
 (2) —substituted or unsubstituted C₁–C₆–alkyl,
 (3) —COOH,
 (4) —halo,
 (5) —OR^{1t}, and
 (6) —NHR^{1t},

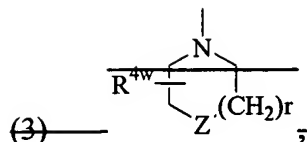
wherein R^{1t} is H or C₁–C₆–alkyl;

R₂ is selected from the group consisting of

- (1) —substituted or unsubstituted aryl,
 (2) —substituted or unsubstituted heteroaryl, and
 (3) —substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) —substituted or unsubstituted C₁–C₆–alkyl,
 (2) —N(R^{1w}, R^{2w}), and



wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H ;
- (b) substituted or unsubstituted $\text{C}_1\text{-C}_6$ -alkyl;
- (c) substituted or unsubstituted aryl;
- (d) substituted or unsubstituted heterocyclyl; and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are

not both H ;

Z is selected from the group consisting of

- (a) O ;
- (b) NR^z ;
- (c) S ;
- (d) SO ;
- (e) SO_2 ; and
- (f) CH_2 ;

wherein R^z is H or substituted or unsubstituted alkyl group; and

R^{4w} is selected from the group consisting of

- (a) H ;
- (b) substituted or unsubstituted $\text{C}_1\text{-C}_6$ -alkyl;
- (c) COOR^{5w} ;
- (d) CONH_2 ;
- (e) OR^{5w} ; and
- (f) NHR^{5w} ;

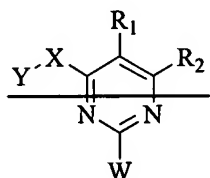
wherein R^{5w} is H or $\text{C}_1\text{-C}_6$ -alkyl; and

r is 0, 1, or 2.

24. (Original) The composition of Claim 23 further comprising at least one additional agent for the treatment of cancer.

25. (Original) The composition of Claim 24, wherein the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, gleevec, herceptin, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab, tamoxifen, CPT 11, and trastuzumab.

26. (Currently amended) A method for treating a condition by modulation of phosphatidylinositol (PI) 3-kinase activity comprising administering to a human or animal subject in need of such treatment an effective amount of a compound ~~having the formula I: of~~ Claim 1.



(I)

~~or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof,~~
wherein

~~Y is selected from the group consisting of~~

- ~~(1) — substituted or unsubstituted C₁-C₆-alkyl,~~
- ~~(2) — substituted or unsubstituted C₂-C₆-alkenyl,~~
- ~~(3) — substituted or unsubstituted C₂-C₆-alkynyl,~~
- ~~(4) — substituted or unsubstituted aryl,~~
- ~~(5) — substituted or unsubstituted heterocyclyl, and~~
- ~~(6) — substituted or unsubstituted heteroaryl;~~

~~X is selected from the group consisting of~~

- ~~(1) — a direct link,~~
- ~~(2) — N(R^{1*}),~~

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(3) — $(\text{CH}_2)_m \text{C}(\text{R}^{2*}, \text{R}^{3*}) \text{N}(\text{R}^{1*})$,

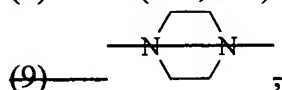
(4) — O,

(5) — S,

(6) — SO,

(7) — SO₂,

(8) — $\text{C}(\text{R}^{2*}, \text{R}^{3*})$, and



wherein R^{1*} , R^{2*} , and R^{3*} are selected from the group consisting of

(a) — H,

(b) — substituted or unsubstituted C₁-C₆-alkyl,

(c) — substituted or unsubstituted C₂-C₆-alkenyl,

(d) — substituted or unsubstituted C₂-C₆-alkynyl,

(e) — substituted or unsubstituted aryl,

(f) — substituted or unsubstituted heterocyclyl,

(g) — substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R_1 is selected from the group consisting of

(1) — H,

(2) — substituted or unsubstituted C₁-C₆-alkyl,

(3) — COOH,

(4) — halo,

(5) — OR^{1t} , and

(6) — NHR^{1t} ,

wherein R^{1t} is H or C₁-C₆-alkyl;

R_2 is selected from the group consisting of

(1) — substituted or unsubstituted aryl,

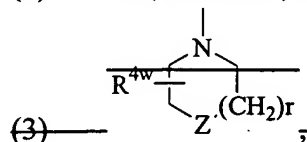
(2) — substituted or unsubstituted heteroaryl, and

(3) — substituted or unsubstituted heterocyclyl; and

~~W is selected from the group consisting of~~

~~(1) substituted or unsubstituted C₁-C₆-alkyl;~~

~~(2) N(R^{1w}, R^{2w}), and~~



~~wherein R^{1w} and R^{2w} are selected from the group consisting of~~

~~(a) H,~~

~~(b) substituted or unsubstituted C₁-C₆-alkyl,~~

~~(c) substituted or unsubstituted aryl,~~

~~(d) substituted or unsubstituted heterocyclyl, and~~

~~(e) substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are~~

~~not both H;~~

~~Z is selected from the group consisting of~~

~~(a) O,~~

~~(b) NR^z,~~

~~(c) S,~~

~~(d) SO,~~

~~(e) SO₂, and~~

~~(f) CH₂,~~

~~wherein R^z is H or substituted or unsubstituted alkyl group; and~~

~~R^{4w} is selected from the group consisting of~~

~~(a) H,~~

~~(b) substituted or unsubstituted C₁-C₆-alkyl,~~

~~(c) COOR^{5w},~~

~~(d) CONH₂,~~

~~(e) OR^{5w}, and~~

~~(f) NHR^{5w},~~

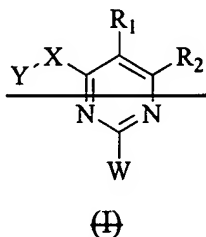
~~wherein R^{5w} is H or C₁-C₆-alkyl; and~~

~~r is 0, 1, or 2.~~

27. (Original) The method of Claim 26, wherein the compound has an IC₅₀ value of less than about 20 µM in a cell proliferation assay.

28. (Original) The method of Claim 26, wherein the condition is cancer.

29. (Currently amended) A method for inhibiting phosphatidylinositol (PI) 3-kinase activity in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound of Claim 1 effective to inhibit phosphatidylinositol (PI) 3-kinase activity in the human or animal subject, ~~wherein the compound has the formula I:~~



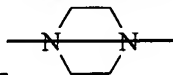
~~or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof,~~
wherein

~~Y is selected from the group consisting of~~

- ~~(1) substituted or unsubstituted C₁-C₆ alkyl,~~
- ~~(2) substituted or unsubstituted C₂-C₆ alkenyl,~~
- ~~(3) substituted or unsubstituted C₂-C₆ alkynyl,~~
- ~~(4) substituted or unsubstituted aryl,~~
- ~~(5) substituted or unsubstituted heterocyclyl, and~~
- ~~(6) substituted or unsubstituted heteroaryl;~~

~~X is selected from the group consisting of~~

- ~~(1) a direct link,~~
- ~~(2) N(R^{1*}),~~
- ~~(3) (CH₂)_m-C(R^{2*}, R^{3*}) N(R^{1*}),~~
- ~~(4) O,~~

- (5) —S—,
 (6) —SO—,
 (7) —SO₂—,
 (8) —C(R^{2*}, R^{3*})—, and
 (9) ——;

wherein R^{1*}, R^{2*}, and R^{3*} are selected from the group consisting of

- (a) —H—,
 (b) —substituted or unsubstituted C₁-C₆-alkyl—,
 (c) —substituted or unsubstituted C₂-C₆-alkenyl—,
 (d) —substituted or unsubstituted C₂-C₆-alkynyl—,
 (e) —substituted or unsubstituted aryl—,
 (f) —substituted or unsubstituted heterocyclyl—,
 (g) —substituted or unsubstituted heteroaryl—; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) —H—,
 (2) —substituted or unsubstituted C₁-C₆-alkyl—,
 (3) —COOH—,
 (4) —halo—,
 (5) —OR^{1t}—, and
 (6) —NHR^{1t}—,

wherein R^{1t} is H or C₁-C₆-alkyl;

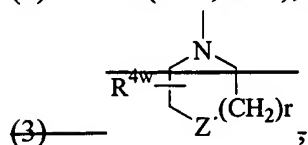
R₂ is selected from the group consisting of

- (1) —substituted or unsubstituted aryl—,
 (2) —substituted or unsubstituted heteroaryl—, and
 (3) —substituted or unsubstituted heterocyclyl—; and

W is selected from the group consisting of

- (1) —substituted or unsubstituted C₁-C₆-alkyl—,

(2) —N(R^{1w}, R^{2w}), and



wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) —H,
- (b) —substituted or unsubstituted C₁-C₆-alkyl,
- (c) —substituted or unsubstituted aryl,
- (d) —substituted or unsubstituted heterocyclyl, and
- (e) —substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are

not both H;

Z is selected from the group consisting of

- (a) —O,
- (b) —NR^z,
- (c) —S,
- (d) —SO,
- (e) —SO₂, and
- (f) —CH₂,

wherein R^z is H or substituted or unsubstituted alkyl group; and

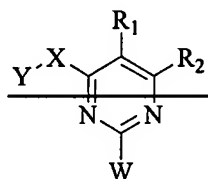
R^{4w} is selected from the group consisting of

- (a) —H,
- (b) —substituted or unsubstituted C₁-C₆-alkyl,
- (c) —COOR^{5w},
- (d) —CONH₂,
- (e) —OR^{5w}, and
- (f) —NHR^{5w},

wherein R^{5w} is H or C₁-C₆-alkyl; and

r is 0, 1, or 2.

30. (Currently amended) A method for treating a cancer disorder in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound of Claim 1 effective to inhibit phosphatidylinositol (PI) 3-kinase activity in the human or animal subject, ~~wherein the compound has the formula I:~~



(I)

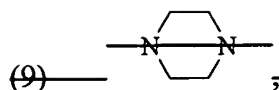
~~or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein~~

~~Y is selected from the group consisting of~~

- ~~(1) — substituted or unsubstituted C₁-C₆-alkyl,~~
- ~~(2) — substituted or unsubstituted C₂-C₆-alkenyl,~~
- ~~(3) — substituted or unsubstituted C₂-C₆-alkynyl,~~
- ~~(4) — substituted or unsubstituted aryl,~~
- ~~(5) — substituted or unsubstituted heterocyclyl, and~~
- ~~(6) — substituted or unsubstituted heteroaryl;~~

~~X is selected from the group consisting of~~

- ~~(1) — a direct link,~~
- ~~(2) — N(R^{1*}),~~
- ~~(3) — (CH₂)_m C(R^{2*}, R^{3*}) N(R^{1*}),~~
- ~~(4) — O,~~
- ~~(5) — S,~~
- ~~(6) — SO,~~
- ~~(7) — SO₂,~~
- ~~(8) — C(R^{2*}, R^{3*}), and~~



wherein R^{1*} , R^{2*} , and R^{3*} are selected from the group consisting of

- (a) H ;
- (b) substituted or unsubstituted C_1-C_6 -alkyl;
- (c) substituted or unsubstituted C_2-C_6 -alkenyl;
- (d) substituted or unsubstituted C_2-C_6 -alkynyl;
- (e) substituted or unsubstituted aryl;
- (f) substituted or unsubstituted heterocyclyl;
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R_1 is selected from the group consisting of

- (1) H ;
- (2) substituted or unsubstituted C_1-C_6 -alkyl;
- (3) $COOH$;
- (4) halo;
- (5) OR^{1t} ; and
- (6) NHR^{1t} ;

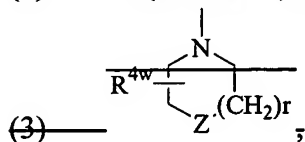
wherein R^{1t} is H or C_1-C_6 -alkyl;

R_2 is selected from the group consisting of

- (1) substituted or unsubstituted aryl;
- (2) substituted or unsubstituted heteroaryl; and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1-C_6 -alkyl;
- (2) $N(R^{1w}, R^{2w})$; and



~~wherein R^{1w} and R^{2w} are selected from the group consisting of~~

- ~~(a) — H,~~
- ~~(b) — substituted or unsubstituted C_1-C_6 -alkyl,~~
- ~~(c) — substituted or unsubstituted aryl,~~
- ~~(d) — substituted or unsubstituted heterocyclyl, and~~
- ~~(e) — substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are~~

~~not both H;~~

~~Z is selected from the group consisting of~~

- ~~(a) — O,~~
- ~~(b) — NR^z ,~~
- ~~(c) — S,~~
- ~~(d) — SO,~~
- ~~(e) — SO_2 , and~~
- ~~(f) — CH_2 ,~~

~~wherein R^z is H or substituted or unsubstituted alkyl group; and~~

~~R^{4w} is selected from the group consisting of~~

- ~~(a) — H,~~
- ~~(b) — substituted or unsubstituted C_1-C_6 -alkyl,~~
- ~~(c) — $COOR^{5w}$,~~
- ~~(d) — $CONH_2$,~~
- ~~(e) — OR^{5w} , and~~
- ~~(f) — NHR^{5w} ,~~

~~wherein R^{5w} is H or C_1-C_6 -alkyl; and~~

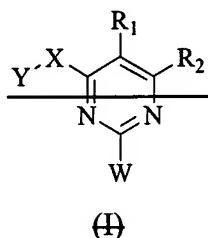
~~r is 0, 1, or 2.~~

31. (Original) The method of Claim 30 further comprising administering to the human or animal subject at least one additional agent for the treatment of cancer.

32. (Original) The method of Claim 31, wherein the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, gleevec, herceptin,

5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab, tamoxifen, CPT 11, and trastuzumab.

33. (Currently amended) A method for inhibiting tumor growth in a human or animal subject, comprising administering to the human or animal subject in need thereof an effective amount of a compound ~~having the formula I:~~ of Claim 1.



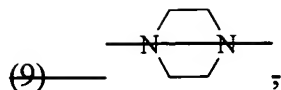
~~or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof,~~
 wherein

~~Y is selected from the group consisting of~~

- ~~(1) substituted or unsubstituted C₁-C₆-alkyl,~~
- ~~(2) substituted or unsubstituted C₂-C₆-alkenyl,~~
- ~~(3) substituted or unsubstituted C₂-C₆-alkynyl,~~
- ~~(4) substituted or unsubstituted aryl,~~
- ~~(5) substituted or unsubstituted heterocyclyl, and~~
- ~~(6) substituted or unsubstituted heteroaryl;~~

~~X is selected from the group consisting of~~

- ~~(1) a direct link,~~
- ~~(2) N(R^{1*}),~~
- ~~(3) (CH₂)_m-C(R^{2*}, R^{3*})-N(R^{1*}),~~
- ~~(4) O,~~
- ~~(5) S,~~
- ~~(6) SO,~~
- ~~(7) SO₂,~~
- ~~(8) C(R^{2*}, R^{3*}), and~~



wherein R^{1*} , R^{2*} , and R^{3*} are selected from the group consisting of

- (a) — H;
- (b) — substituted or unsubstituted C_1 - C_6 -alkyl;
- (c) — substituted or unsubstituted C_2 - C_6 -alkenyl;
- (d) — substituted or unsubstituted C_2 - C_6 -alkynyl;
- (e) — substituted or unsubstituted aryl;
- (f) — substituted or unsubstituted heterocyclyl;
- (g) — substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R_1 is selected from the group consisting of

- (1) — H;
- (2) — substituted or unsubstituted C_1 - C_6 -alkyl;
- (3) — $COOH$;
- (4) — halo;
- (5) — OR^{1t} ; and
- (6) — NHR^{1t} ;

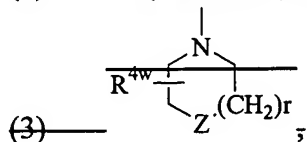
wherein R^{1t} is H or C_1 - C_6 -alkyl;

R_2 is selected from the group consisting of

- (1) — substituted or unsubstituted aryl;
- (2) — substituted or unsubstituted heteroaryl; and
- (3) — substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) — substituted or unsubstituted C_1 - C_6 -alkyl;
- (2) — $N(R^{1w}, R^{2w})$; and



~~wherein R^{1w} and R^{2w} are selected from the group consisting of~~

- ~~(a) — H,~~
- ~~(b) — substituted or unsubstituted C_1-C_6 -alkyl,~~
- ~~(c) — substituted or unsubstituted aryl,~~
- ~~(d) — substituted or unsubstituted heterocyclyl, and~~
- ~~(e) — substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are~~

~~not both H;~~

~~Z is selected from the group consisting of~~

- ~~(a) — O,~~
- ~~(b) — NR^z ,~~
- ~~(c) — S,~~
- ~~(d) — SO,~~
- ~~(e) — SO_2 , and~~
- ~~(f) — CH_2 ,~~

~~wherein R^z is H or substituted or unsubstituted alkyl group; and~~

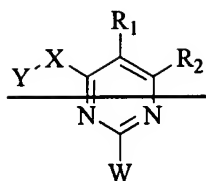
~~R^{4w} is selected from the group consisting of~~

- ~~(a) — H,~~
- ~~(b) — substituted or unsubstituted C_1-C_6 -alkyl,~~
- ~~(c) — $COOR^{5w}$,~~
- ~~(d) — $CONH_2$,~~
- ~~(e) — OR^{5w} , and~~
- ~~(f) — NHR^{5w} ,~~

~~wherein R^{5w} is H or C_1-C_6 -alkyl; and~~

~~r is 0, 1, or 2.~~

34. (Currently amended) A method for inhibiting the proliferation of capillaries in a human or animal subject, comprising administering to the human or animal subject in need thereof an effective amount of a compound ~~having the formula I: of Claim 1.~~



(I)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof,

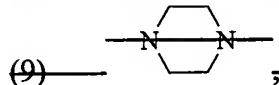
wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C₁-C₆-alkyl;
- (2) substituted or unsubstituted C₂-C₆-alkenyl;
- (3) substituted or unsubstituted C₂-C₆-alkynyl;
- (4) substituted or unsubstituted aryl;
- (5) substituted or unsubstituted heterocyclyl; and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link;
- (2) N(R^{1*});
- (3) (CH₂)_m-C(R^{2*}, R^{3*})-N(R^{1*});
- (4) O;
- (5) S;
- (6) SO;
- (7) SO₂;
- (8) C(R^{2*}, R^{3*}); and



wherein R^{1*}, R^{2*}, and R^{3*} are selected from the group consisting of

- (a) H;
- (b) substituted or unsubstituted C₁-C₆-alkyl;
- (c) substituted or unsubstituted C₂-C₆-alkenyl;

- (d) ~~substituted or unsubstituted C₂-C₆-alkynyl,~~
- (e) ~~substituted or unsubstituted aryl,~~
- (f) ~~substituted or unsubstituted heterocyclyl,~~
- (g) ~~substituted or unsubstituted heteroaryl; and~~

~~m is 0, 1, 2, 3, or 4;~~

~~R₁ is selected from the group consisting of~~

- (1) ~~H,~~
- (2) ~~substituted or unsubstituted C₁-C₆-alkyl,~~
- (3) ~~COOH,~~
- (4) ~~halo,~~
- (5) ~~OR^{1t}, and~~
- (6) ~~NHR^{1t},~~

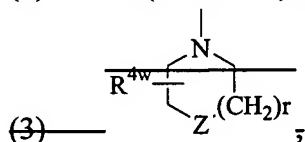
~~wherein R^{1t} is H or C₁-C₆-alkyl;~~

~~R₂ is selected from the group consisting of~~

- (1) ~~substituted or unsubstituted aryl,~~
- (2) ~~substituted or unsubstituted heteroaryl, and~~
- (3) ~~substituted or unsubstituted heterocyclyl; and~~

~~W is selected from the group consisting of~~

- (1) ~~substituted or unsubstituted C₁-C₆-alkyl,~~
- (2) ~~N(R^{1w}, R^{2w}), and~~



~~wherein R^{1w} and R^{2w} are selected from the group consisting of~~

- (a) ~~H,~~
- (b) ~~substituted or unsubstituted C₁-C₆-alkyl,~~
- (c) ~~substituted or unsubstituted aryl,~~
- (d) ~~substituted or unsubstituted heterocyclyl, and~~

~~(e) substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are not both H;~~

~~Z is selected from the group consisting of~~

- ~~(a) O,~~
- ~~(b) NR^z,~~
- ~~(c) S,~~
- ~~(d) SO,~~
- ~~(e) SO₂, and~~
- ~~(f) CH₂,~~

~~wherein R^z is H or substituted or unsubstituted alkyl group; and~~

~~R^{4w} is selected from the group consisting of~~

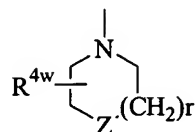
- ~~(a) H,~~
- ~~(b) substituted or unsubstituted C₁-C₆-alkyl,~~
- ~~(c) COOR^{5w},~~
- ~~(d) CONH₂,~~
- ~~(e) OR^{5w}, and~~
- ~~(f) NHR^{5w},~~

~~wherein R^{5w} is H or C₁-C₆-alkyl; and~~

~~r is 0, 1, or 2.~~

- 35. (Canceled)
- 34. (Canceled) Redundant Claim. Same as Claim 34.
- 36. (Canceled)
- 37. (New) A compound of Claim 1, wherein R₂ is hydroxy-substituted phenyl.
- 38. (New) A compound of Claim 1, wherein R₂ is substituted or unsubstituted pyridinyl.
- 39. (New) A compound of Claim 1, wherein R₂ is substituted or unsubstituted pyrimidinyl.

40. (New) A compound of Claim 1, wherein W is



41. (New) A compound of Claim 40, wherein R^{4w} is H, r is 1, and Z is O.

42. (New) A compound of Claim 1, wherein Y is substituted or unsubstituted heterocyclyl.

43. (New) A compound of Claim 1, wherein X is a O and Y is substituted or unsubstituted heterocyclyl.

44. (New) A compound of Claim 1, wherein X is a direct link and Y is substituted or unsubstituted heterocyclyl.

45. (New) A compound of Claim 40, wherein R^{4w} is H, r is 1, Z is O, Y is substituted or unsubstituted heterocyclyl, R₁ is H, and R₂ is substituted or unsubstituted heteroaryl.

46. (New) A compound of Claim 40, wherein R^{4w} is H, r is 1, Z is O, X is O or a direct link, Y is substituted or unsubstituted heterocyclyl, R₁ is H, and R₂ is substituted or unsubstituted heteroaryl.